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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/304,121	05/03/99	VOELLMY R	870109.409

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RICHARD G SHARKEY
SEED AND BERRY LLP
6300 COLUMBIA CENTER
701 FIFTH AVENUE
SEATTLE WA 98104-7092

EXAMINER	
SATISH,J	
ART UNIT	**PAPER NUMBER**
1645	10

DATE MAILED: 03/13/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/304,121	Vollemy, Richard
Examiner	**Group Art Unit**
Jaya Satish,Ph.D.	1645

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-35* is/are pending in the application.

Of the above, claim(s) *34* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-33 and 35* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892 ✓

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 8 ✓

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948 ✓

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Election/Restriction

Applicant's election without traverse of Group I (claims 1-33 and 35) in Paper No.9, dated 2/12/00 is acknowledged and has been entered. Claim 34 is withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention. Claims 1-33 and 35 are currently under prosecution.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-2, 7-26, 28-33 and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Moonen Chrit (WO 98/06864, 19.02.98).

Summary of Invention: Claims 1-2, 7-26, 28-33 and 35 recite four types of molecular circuits comprising sequence elements as recited in independent claims 1(a,b), 9(a,b,c), 15(a,b,c), 22(a,b), comprising nucleic acid molecules that comprises a gene encoding a transcription factor operably linked to a promoter sequence, an expression vector or a set of expression vectors comprising the molecular circuits, a recombinant eukaryotic host cell comprising the

expression vector recited in any one of claims 7,12, 18 or 24 or an expression vector set recited in any one of claims 8,13, 14, 19, 20 or 25, or a virus recited in claim 30, comprising the expression vector or a pharmaceutical composition comprising a virus recited in claim 30 and a pharmaceutically acceptable carrier.

Moonen Chrit discloses genetically engineered constructs comprising a nucleic acid of interest or a selected gene operably linked to a promoter (constitutive or inducible), preferably a heat shock protein (HSP), incorporating the construct into an expression vector and introducing the vector into a suitable host cell, target cell or organism. A subset of recombinant or transformed cells that occupy selected spatial coordinates are heated to activate the promoter and express the gene. Moonen Chrit teaches that the specific transcription factor activated during heat shock is often referred to as HSF-1. Moonen Chrit teaches that HSP-1 trimerizes during stress mediated by HSP 70 and then binds to a consensus nucleotide sequence, the heat shock element (HSE), located within the promoter element of the HSP genes.

Moonen Chrit teaches that vectors typically comprise a eukaryotic transcription unit or an expression cassette that contains all the elements required for the expression of exogenous genes in eukaryotic cells. A typical expression cassette contains a promoter operably linked to the DNA sequence encoding a desired protein and transcription and translation initiation sequences for the regulation of expression of the particular nucleic acid.

Moonen Chrit teaches the use of cloning vectors such as retroviral vectors, adeno-associated viral vectors (AAVs), recombinant AAV (rAAV) vectors, plasmids, non-pathogenic vectors

derived from HIV, as gene delivery systems. Moonen Chrit teaches pharmaceutical compositions comprising selected vectors and suitable carriers containing selected nucleic acids for *in vivo* administration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moonen Chrit as applied to claims 1-2, 7-26, 28-33 and 35 above, and further in view of Zuo et al (Molecular and Cellular Biology, Aug. 1995, 15(8): 4319-4330).

Summary of Invention: Claims 3-6, recite a molecular circuit of claim 1 wherein the heat shock transcription factor (HSF) is a mutated HSF or a chimeric HSF. The HSF is derived from a vertebrate (mammalian or avian) or from an insect.

The teachings of Moonen Chrit have been set forth above. Moonen Chrit does not expressly disclose a mutated or chimeric heat shock transcription factor (HSF) derived from a vertebrate (mammalian or avian) or from an insect.

Zuo et al teach expression constructs with wild-type HSF gene, a mutant human or hHSF1 gene as well as a chimeric LexA(87)-hHSF1(79) gene.

Given that, Moonen Chrit has taught genetically engineered molecular constructs and eukaryotic expression cassettes containing all the elements required for the expression of exogenous genes in eukaryotic cells, and that Zuo et al have taught expression constructs with wild type, mutant and chimeric hHSF1 gene, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Moonen Chrit and Zuo et al and construct expression vectors sets with molecular circuits to stimulate the expression of the gene of interest. One of ordinary skill in the art would have been motivated at the time the invention was made to generate a recombinant host cell comprising the expression vector and expose the recombinant host cell to stress in vitro by heat treatment or administer *in vivo* a pharmaceutical composition comprising the expression vector and stimulate the gene of interest by application of selective or localized stress as taught by Moonen Chrit.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moonen Chrit as applied to claims 1-2, 7-26, 28-33 and 35 above, and further in view of Bailey et al (In Methods in Molecular Biology Vol 7 : Gene Transfer and Expression Protocols, Murray (ed) pages 147-168, The Humana Press, Inc. 1991).

Summary of Invention: Claim 27 recites a method of producing a protein of interest comprising the steps of culturing the recombinant host cell of claim 26, stimulating the first

promoter by exposing the recombinant cells to stress and isolating the protein of interest expressed by the gene of interest.

Bailey et al teach established techniques for producing recombinant proteins in baculovirus systems.

Given that, Moonen Chrit has taught genetically engineered molecular constructs and eukaryotic expression cassettes containing all the elements required for the expression of exogenous genes in eukaryotic cells, and that Zuo et al have taught expression constructs with wild type, mutant and chimeric hHSF1 gene, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Moonen Chrit and Zuo et al and construct a set of expression vectors comprising molecular circuits comprising wild type, mutant or chimeric HSF1 genes or pharmaceutical compositions comprising expression vectors or recombinant host cell comprising expression vectors and stimulate the gene of interest by application of selective or localized stress to provide a therapeutic protein to selected cells in an animal as taught by Moonen Chrit. One of ordinary skill in the art would have been motivated at the time the invention was made to produce a protein by established recombinant methods as taught by Bailey et al, by culturing recombinant host cells, stimulating the gene of interest by exposing cultured cells to heat treatment and isolating the protein of interest expressed by the gene of interest.

The subject matter of the claimed invention is *prima facie* obvious.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jaya Satish at (703) 306 9047. The examiner can normally be reached, Monday through Friday from 9.00 AM to 4.00 PM. If attempts to reach the examiner by telephone are unsuccessful, a supervisory examiner, Anthony Caputa can be reached at (703) 305 -3995. Any inquiry of a general nature should be directed to the Group receptionist at (703) 308-1235. Papers relating to this application may be faxed to Technology Center 1600 at (703) 305-3592. Any documents submitted by fax transmission will be considered an official communication unless the cover sheet clearly indicates that it is an informal communication.

JS

Jaya Satish, Ph.D.

March 7, 2000

Gary L. Kunz

GARY L. KUNZ
PRIMARY EXAMINER
GROUP 1200